

human health effects are lacking and animal or laboratory studies are used to assess risk. The literature review provides the SAB with the information necessary to classify a compound's effects as carcinogenic or noncarcinogenic (or both).

**Dose-Response Assessment:** The dose-response relationship describes the correlation between extent of exposure to an agent (dose) and the resulting effects (response). A dose-response curve can then be developed for a given chemical to the extent that this relationship is described in the literature. This type of exercise is necessary to correlate high-level experimental type exposures to the types of exposures that are more likely to take place in the environment. Often toxic agents will give rise to a variety of adverse health effects. In these cases an effort is made to establish a dose-response relationship for each effect so that a comparison of potency can be undertaken. Generally the SAB aims to protect against the most sensitive effect since this level of protection will also be protective for other, less sensitive endpoints. The dose-response data in the literature may be from human or animal studies, and may provide information regarding mechanism of action of the toxicant. In general, the SAB uses different risk assessment methods when considering noncarcinogenic and carcinogenic effects of compounds.

Noncarcinogens : The potential for an adverse health effect due to exposure to noncarcinogenic compounds is related to the dose of the compound. The SAB examines the dose-response data from the literature, thus developing an impression of the shape of the dose-response curve. Identifying this dose-response relationship aids in extrapolating from experimental doses to those that are likely to be found in the ambient air.

The SAB risk assessments for noncarcinogens are often based on the No Observed Adverse effect Level (NOAEL) reported in the peer-reviewed literature. If there is not a NOAEL reported, the Lowest Observed Adverse Effect Level (LOAEL) may be converted to a NOAEL using an uncertainty factor. In cases where a NOAEL is determined in experimental animal systems, an additional uncertainty factor might be implemented to compensate for potential differences between humans' and laboratory animals' body size, metabolic rates and lifespans. Since there is also a widely recognized variability in interindividual sensitivity, an uncertainty factor may be employed to protect especially sensitive human subpopulations. Default assumptions for conversion from experimental data to safe human exposure levels that are used by the EPA and others include a 10-fold factor for LOAEL to NOAEL conversion, a factor of 10 for extrapolation from animal data to human and another factor of 10 to account for variability in human susceptibility.

Mechanistic data are used by the SAB whenever possible to move away from default assumptions. The dose-response relationship and the severity of the adverse effect are considered by the SAB in determining the appropriate uncertainty factor to be used in converting a LOAEL to a NOAEL. This allows the SAB to use all the data available and move away from the default factor of 10 if the data warrant. A factor of 10 is used by the SAB for LOAEL to NOAEL conversion if the dose-response curve is broad and the effect is severe. A factor of 5 is used if the dose-response curve is broad, and a factor of 2 may be used if the dose-response curve is steep. In a similar fashion, there is some flexibility in the safety factors that are used to compensate for interspecies or interindividual variability. The appropriate safety factors to be used are determined on a case-by-case basis. A table of uncertainty factors used by the SAB follows the text of this document.

Carcinogens: The potential cancer risk in a human population resulting from exposure to a carcinogenic substance is related to exposure dose. The EPA estimates potential risk due to exposure to a given